

Complete Summary

GUIDELINE TITLE

Position statement on lipid management--2005.

BIBLIOGRAPHIC SOURCE(S)

Tonkin A, Barter P, Best J, Boyden A, Furler J, Hossack K, Sullivan D, Thompson P, Vale M, Cooper C, Robinson M, Clune E, National Heart Foundation of Australia, Cardiac Society of Australia and New Zealand. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: position statement on lipid management--2005. Heart Lung Circ 2005 Dec;14(4):275-91. [70 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Lipid Management Guidelines—2001 (supplement). Med J Aust 2001;175:S57-88.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Cardiovascular disease (CVD)

GUIDELINE CATEGORY

Management
Prevention

Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for best practice in lipid management for health practitioners, patients, and policy makers

TARGET POPULATION

Individuals with a higher absolute risk of a cardiovascular disease (CVD) event, including the following:

- Those with clinical evidence of:
 - Vascular disease including coronary heart disease, stroke, peripheral arterial disease
 - Diabetes mellitus (including diagnostic biochemical criteria)
 - Chronic kidney disease
 - Familial hypercholesterolaemia
- Aboriginal and Torres Strait Islander peoples
- Those with absolute risk of $\geq 15\%$ of a CVD event in the next 5 years using 1991 Framingham equation (e.g., New Zealand CVD absolute risk calculator)
- Those with absolute risk of 10–15% of a CVD event in the next 5 years when any of the following is present:
 - Family history of premature coronary heart disease (CHD) (first degree relative who developed coronary heart disease before age 60)
 - The metabolic syndrome (in which central adiposity is now considered to be of paramount importance)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Risk assessment
2. Management:
 - Lifestyle measures including dietary modification
 - Initiation of lipid modifying therapy
3. Other, new combined therapies
4. Targets
5. Safety
6. Implementation and the gap between evidence and treatment
7. Considerations for disadvantaged groups

MAJOR OUTCOMES CONSIDERED

- Mortality
- Rates of cardiovascular events
- Adverse effects of therapy
- Low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

II: Evidence obtained from at least one properly designed randomised controlled trial

III-1: Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)

III-2: Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group

III-3: Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series with parallel control group

IV: Evidence obtained from case series, either post-test or pre-test and post-test

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The position statement has been developed primarily by an Executive Writing Group nominated by the Cardiac Society of Australia and New Zealand (CSANZ) and the Clinical Issues Committee and the Nutrition and Metabolism Advisory Committee of the National Heart Foundation of Australia (NHFA) using a consensus approach.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

- A. Rich body of high-quality randomized controlled trial (RCT) data (Level of evidence I)
- B. Limited body of RCT data or high-quality non-RCT data (level of evidence, II, III-1, III-2)
- C. Limited evidence (level of evidence III-3, IV)
- D. No evidence available – panel consensus judgment (expert opinion)

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A range of lipid, cardiovascular and general practice and other experts and organisations were invited to comment on drafts. After considering comments received the draft was modified by the Executive Writing Group and then reviewed and approved by the National Heart Foundation of Australia (NHFA) and Cardiac Society of Australia and New Zealand (CSANZ).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the Levels of Evidence (I, II, III-1, III-2, III-3, IV) and Grades of Recommendation (A–D) are given at the end of the Major Recommendations field.

This 2005 position statement aims to serve as an interim update to the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand Lipid Management Guidelines—2001, pending a fuller review when other clinical trial

data are available. Refer to Table 1 in the original guideline document for a listing of the important changes to the 2001 guideline.

Key Messages and Summary of Recommendations

Risk Assessment

In order to initiate the most cost-effective cardiovascular disease (CVD) risk factor management strategies, it is necessary to identify those individuals at higher absolute risk of a CVD event, and who therefore have the most to benefit.

The groups at higher risk are:

- Those with clinical evidence of:
 - Vascular disease including coronary heart disease, stroke, peripheral arterial disease
 - Diabetes mellitus (including diagnostic biochemical criteria)
 - Chronic kidney disease
 - Familial hypercholesterolaemia
- Aboriginal and Torres Strait Islander peoples
- Those with absolute risk of $\geq 15\%$ risk of a CVD event in the next 5 years using 1991 Framingham equation (e.g., New Zealand CVD absolute risk calculator)
- Those with absolute risk of 10–15% of a CVD event in the next 5 years when any of the following is present:
 - Family history of premature coronary heart disease (CHD) (first degree relative who developed CHD before age 60)
 - The metabolic syndrome (in which central adiposity is now considered to be of paramount importance)

Management

Lifestyle Measures

- Lifestyle interventions, including attention to dietary modification, must underpin lipid management in all people. **(I A)**

Initiation of Lipid-Modifying Therapy

Vascular Disease

- Statin therapy is recommended for all people with clinical evidence of vascular disease (coronary heart disease, stroke, peripheral arterial disease) and should be commenced in hospital for those admitted with coronary heart disease events. **(I A)**
- Fibrates could be considered in combination with statins, particularly in those with manifestations of the metabolic syndrome (high triglyceride levels, low high-density lipoprotein cholesterol [HDL-C] levels, and/or those who are overweight). **(I A)**

Diabetes

- Those with type 2 diabetes who have a low-density lipoprotein cholesterol (LDL-C) >2.5 mmol/L after interventions to modify lifestyle and improve blood glucose control should be considered for statin therapy. **(II B)**
- Those with type 2 diabetes who have triglycerides >2.0 mmol/L after interventions to modify lifestyle and improve blood glucose control should be considered for fibrate therapy. **(II B)**

Chronic Kidney Disease

Pending the results of trials it is recommended that the decision to start treatment with a statin for people with kidney impairment be made on an individual basis. **(C)**

Familial Hypercholesterolaemia

Statin therapy recommended. **(B)**

Aboriginal and Torres Strait Islander People

Commence screening for lipid levels at 18 years of age, and consider statin therapy if LDL-C >2.5 mmol/L after lifestyle modification. **(C)**

Others with Elevated Absolute Risk of CVD **(C)**

Lipid-modifying therapy is indicated for those with:

- Absolute risk $\geq 15\%$ of a CVD event in the next 5 years *or*
- Absolute risk 10–15% of a CVD event in the next 5 years when either of the following is present:
 - Family history of premature CHD (first degree relative who developed CHD before age 60)
 - The metabolic syndrome

Pharmaceutical Benefits Scheme (PBS) criteria for eligibility for subsidy should be taken into account, particularly for those assessed to be in the lower risk group described above.

Age

Although the 1991 Framingham equation is not reliable for use in people over 70 years, older individuals are at higher absolute risk of future CVD events compared to younger individuals and it is important that drug therapy is not withheld on the basis of age alone. **(B)**

Other, New and Combined Therapies

- Fibrates are known to reduce coronary risk, especially in people with type 2 diabetes or with features of the metabolic syndrome, and can be considered in combination with a statin to achieve both HDL-C raising and LDL-C lowering. However, the risk of myopathy must be considered, particularly with

- the combination of gemfibrozil and a statin. The risk of myopathy is lower with the combination of fenofibrate and a statin. **(II B)**
- Ezetimibe is a member of a new class of drugs that inhibit the absorption of cholesterol by the intestine. It is well tolerated, and reduces the concentration of LDL-C by 15–20% when given either as monotherapy or when added to a statin. Further long-term safety data are awaited, particularly relating to the combination of ezetimibe and a statin. **(II B)**

Targets

- LDL-C

Recent trials have demonstrated the benefit of lowering LDL-C to levels substantially below the current recommended target of <2.5 mmol/L in high-risk patients with existing CHD. The results of these trials support a target LDL-C of <2.0 mmol/L for this patient population. The validity of this suggestion will be reviewed in the light of results of trials currently in progress. **(II B)**

- High-density lipoprotein cholesterol >1.0 mmol/L **(B)**
- Triglycerides <1.5 mmol/L **(B)**
- Other potential targets:
 - Levels of C-reactive protein (CRP) are independently related to risk of future CHD events. However, due to insufficient data to indicate the benefit of targeting CRP with treatment, it is premature to use CRP routinely in the assessment of CVD risk, or to propose a particular goal for treatment. **(D)**
 - It is anticipated that future guidelines will ascribe greater importance to apolipoprotein B (or non-high-density lipoprotein cholesterol as a lesser alternative), particularly in those individuals who have elevated triglyceride levels. **(D)**

Safety

- In general, current cholesterol-modifying treatments are well tolerated and very safe.
- The risk of rhabdomyolysis should be borne in mind with statins, especially with higher-dose, long term therapy.
 - It is recommended that creatine kinase (CK) is measured at commencement of therapy and, if suggestive muscle symptoms are reported, it is measured again with blood levels compared to the earlier measurement.
 - Routine monitoring of creatine kinase is not recommended, although particular caution and monitoring is appropriate for patients taking particular concomitant medications and those of advanced age or with kidney dysfunction.
 - Statin therapy should be suspended for the duration of treatment with macrolide antibiotics.
- The risk of rhabdomyolysis is increased with statin/fibrate combination therapy, particularly with gemfibrozil.
- The incidence of statin-related elevation of hepatic enzymes in clinical trials has ranged from 0 to 0.8% and is dose-dependent. Modest elevations of

alanine transferase (ALT) are common and usually settle on cessation or lowering of dose.

- There is no evidence that statins increase the risk of cancer.
- Despite case reports of memory impairment with statins, available trial data have shown no evidence of statin-induced changes in formal tests of neuropsychological function.
- Ezetimibe appears to be well tolerated; however, further long-term safety data are awaited, particularly relating to ezetimibe/statin combination therapy.

Implementation and the Gap Between Evidence and Treatment

- Only a minority of patients with CHD achieve the target levels for their modifiable risk factors due to patient-related, doctor-related, and other factors.
- Measures to overcome the gap between the evidence base and practice include in-hospital initiation of treatment, recall systems, and alternative systems of care (e.g., coaching).
- Once at target, all patients at high risk should have their lipid levels measured every 6–12 months as part of the ongoing assessment of adherence and management of overall cardiovascular risk.

Disadvantaged Groups

- There is an independent association between cardiovascular death and disease incidence and markers of socioeconomic position.
- The gap between evidence and practice may be greater for some disadvantaged communities both with respect to prescribing (doctor) and adherence (patient) factors.
- Although aspects of socioeconomic position are not considered in absolute risk equations, these factors are important in suggesting the need for particular measures to support appropriate treatment and treatment adherence.
- The use of multidisciplinary teams in general practice has been identified as an important way to overcome the barriers faced by doctors and patients in providing high quality preventive care in disadvantaged areas.

Definitions:

Levels of Evidence

I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

II: Evidence obtained from at least one properly designed randomised controlled trial

III-1: Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)

III-2: Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group

III-3: Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series with parallel control group

IV: Evidence obtained from case series, either post-test or pre-test and post-test

Grades of Recommendations

- A. Rich body of high-quality randomized controlled trial (RCT) data (Level of evidence I)
- B. Limited body of RCT data or high-quality non-RCT data (level of evidence, II, III-1, III-2)
- C. Limited evidence (level of evidence III-3, IV)
- D. No evidence available – panel consensus judgment (expert opinion)

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is specifically stated for selected recommendations.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of lifestyle and pharmacologic interventions for lipid management in individuals with a higher absolute risk of a cardiovascular disease event

POTENTIAL HARMS

- The combination of fibrates and statins has been reported to be associated with a small but significant risk of myopathy.
- The risk of rhabdomyolysis should be borne in mind with statins, especially with higher-dose, long term therapy.
- The risk of rhabdomyolysis is increased with statin/fibrate combination therapy, particularly with gemfibrozil.
- The incidence of statin-related elevation of hepatic enzymes in clinical trials has ranged from 0 to 0.8% and is dose-dependent. Modest elevations of alanine transferase (ALT) are common and usually settle on cessation or lowering of dose.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and the Gap between Evidence and Treatment

The Evidence-Treatment Gap

Evidence from Australian as well as international surveys indicates that only a minority of patients with coronary heart disease (CHD) achieve the target levels for their modifiable risk factors or even receive treatment. There are three possible reasons for this treatment gap: patients may not attend the doctor; doctors may not prescribe appropriate treatment; and/or there may be poor patient adherence to treatment regimens. Possible solutions to overcome the gap between the evidence base and actual practice are shown in Table 5 in the original guideline document. Some of these measures are directed towards the treating doctors and some at the patients.

The Importance of Monitoring

The Cochrane Collaboration systematic review of interventions for helping patients to follow prescriptions for (all) medications clearly shows that measures to improve adherence are inseparably bound to achievement of the clinical goals for which the drugs are prescribed. This suggests it may be very relevant to measure the short term outcomes of effective treatments such as measures of cardiovascular risk factors. For cardiovascular disease, perhaps the most clinically relevant of these are the regular measurement of serum lipids. All patients at high risk should have their lipid levels measured every 6–12 months as part of the ongoing assessment of adherence and management of overall cardiovascular risk.

Other Methods of Improving Adherence

Particularly noteworthy are the importance of in-hospital initiation of treatment, recall systems, and disease management systems which empower the patient. An example of the latter, which has been successfully initiated in Australia, is The COACH Program—a training program for patients with CHD in which a health professional 'coach' trains the patient to vigorously pursue the target levels for their risk factors whilst working in partnership with their own doctors.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Tonkin A, Barter P, Best J, Boyden A, Furler J, Hossack K, Sullivan D, Thompson P, Vale M, Cooper C, Robinson M, Clune E, National Heart Foundation of Australia, Cardiac Society of Australia and New Zealand. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: position statement on lipid management--2005. *Heart Lung Circ* 2005 Dec;14(4):275-91. [70 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 (revised 2005 Dec)

GUIDELINE DEVELOPER(S)

Cardiac Society of Australia and New Zealand - Disease Specific Society
National Heart Foundation of Australia - Disease Specific Society

SOURCE(S) OF FUNDING

National Heart Foundation of Australia
Cardiac Society of Australia and New Zealand

GUIDELINE COMMITTEE

Executive Writing Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Group Members: Prof. Andrew Tonkin (*Chair*); Prof. Philip Barter; Prof. James Best; Dr. Andrew Boyden; Dr. John Furler; Dr. Ken Hossack; A/Prof. David Sullivan; Prof. Peter Thompson; Dr. Margarite Vale; Ms. Catherine Cooper (Executive Officer until December 2004); Ms. Malia Robinson (Executive Officer from January to May 2005); Ms. Eleanor Clune (Executive Officer from June 2005)

Other Contributors: Terry Campbell, Cardiac Society of Australia and New Zealand; David Colquhoun; Sophie Couzos, National Aboriginal Community Controlled Health Organisation; Anthony Dart; Marcia George, Royal College of Nursing, Australia; Pamela Horsely, Dietitians' Association of Australia; Michael Jelinek; Garry Jennings; Elspeth Kay, National Prescribing Service; Paul Nestel; Manny Noakes; Craig Patterson, National Prescribing Service; Ian Scott, Internal Medicine Society of Australia & New Zealand; Leon Simons; Vanessa Simpson, National Prescribing Service; Robert Walker, Kidney Health Australia; Harvey White, Cardiac Society of Australia and New Zealand

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Philip Barter has been involved in research initiated by AstraZeneca, Pfizer, Fournier, GlaxoSmithKline and Merck Sharpe & Dohme. He has been involved in research funded by Pfizer and has acted in an advisory capacity, or received travel assistance or fees for service from AstraZeneca, Pfizer, Merck Sharpe & Dohme, Fournier and Merck Pharma (UK).

James Best has been involved in research funded by Eli Lilly, Laboratoires Fournier and Pfizer, and acted in an advisory capacity or received travel assistance or fees for service from AstraZeneca, Pfizer, Merck Sharpe & Dohme, Aventis, Eli Lilly and Laboratoires Fournier.

John Furler has been involved in research funded by Pfizer.

David Sullivan has been involved in research initiated by Pfizer, AstraZeneca and Merck Sharpe & Dohme and research funded by Aventis. He has acted in an advisory capacity or received travel assistance or fees for service from AstraZeneca, Merck Sharpe & Dohme, Pfizer and Novartis.

Peter Thompson has been involved in research initiated by Pfizer and acted in an advisory capacity or received travel assistance or fees for service from Bristol-Myers Squibb, Pfizer and AstraZeneca.

Andrew Tonkin has received research funding from AstraZeneca, Bristol-Myers Squibb and Fournier, been involved in research initiated by Merck Sharpe & Dohme, and acted in an advisory capacity or received travel assistance or fees for service from AstraZeneca, Bristol-Myers Squibb, Pfizer, Sankyo, Fournier and Servier. Margerite Vale has received part funding for research from Merck Sharpe & Dohme.

Andrew Boyden, Eleanor Clune, Catherine Cooper, Ken Hossack and Malia Robinson have no conflicts of interest to declare.

ENDORSER(S)

Australian Atherosclerosis Society - Disease Specific Society
Internal Medicine Society of Australia and New Zealand - Medical Specialty Society
Kidney Health Australia - Professional Association
National Prescribing Service - National Government Agency [Non-U.S.]
National Stroke Foundation (Australia) - Professional Association
Royal Australian College of General Practitioners - Professional Association
Royal College of Nursing Australia - Professional Association

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Lipid Management Guidelines—2001 (supplement). Med J Aust 2001;175:S57–88.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [National Heart Foundation of Australia](#).

Print copies: Available from the National Heart Foundation of Australia's national telephone information service at 1300 36 27 87 or E-mail: heartline@heartfoundation.com.au.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 5, 2007. The information was verified by the guideline developer on June 27, 2007.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline.

Copyright for the original guideline/evidence review remains with the National Heart Foundation of Australia. The content contained within the original guideline/evidence review may not be reproduced in any form or language without permission from the National Heart Foundation of Australia. Before applying for permissions, request for the copyright terms and conditions document from copyright@heartfoundation.com.au. In addition, content contained within the original guideline and/or the NGC summary of this guideline may not be used for commercial and/or product endorsement.

© 2005 Australasian Society of Cardiac and Thoracic Surgeons and the Cardiac Society of Australia and New Zealand

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 9/15/2008

